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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/762,581	01/23/2004	Steven N. Mink	82402-10302	3020

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EXAMINER	
KHARE, DEVESH	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 12/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/762,581	MINK ET AL.	
	Examiner	Art Unit	
	Devesh Khare	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/9/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's election of the claims of Group II corresponding to claims 1-16 in the reply filed on 09/20/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is therefore made FINAL.

Claims 17 and 18 have been cancelled.

An action on the merits of claims 1-16 is contained herein below.

35 U.S.C. 112, first paragraph rejection

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-16 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of myocardial dysfunction and an inflammatory response, does not reasonably provide enablement for a method of preventing or reducing the myocardial dysfunction and an inflammatory response by administering to a cell or animal in need thereof an effective amount of an agent and while being enabling for inhibitory effects of N,N' diacetylchitobiose as an inhibitor of lysozyme, does not reasonably provide enablement for any agent that can inhibit lysozyme to a cell or animal in need thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

The factors regarding undue experimentation have been summarized in *In re Wands,* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

(1) The quantity of experimentation necessary (time and expense);

(2) The amount of direction or guidance presented;

(3) The presence or absence of working examples of the invention;

(4) The nature of the invention;

(5) The state of the prior art;

(6) The predictability or unpredictability of the art;

(7) The breadth of the claims; and

(8) The relative skill of those in the art.

With regard to factors (1) and (2) cited above, undue experimentation is required to determine how an agent can be used to a cell or animal in need thereof for a method of preventing or reducing the myocardial dysfunction and an inflammatory response and to inhibit lysozyme. There has not been provided adequate guidance in the written description for accomplishing such, as only the treatment of myocardial dysfunction and

an inflammatory response and inhibitory effects of N,N' diacetylchitobiose as an inhibitor of lysozyme were described.

With regard to factors (4), (5) and (6), it is noted that there is a great deal of unpredictability in the art. For example, Rubio et al. teach effects of two lysozyme competitive inhibitors, histamine and N-acetyl-D-glucosamine in the formation of the enzyme-inhibitor complex (see abstract) and Valisena et al. teach the effects of egg-white lysozyme inhibitors such as heparin, histidine methylester, chitotriose and chitobiose on immune response (abstract). The arts at the time the invention was made fails to establish predictability with regard to an agent of the applicant's which can inhibit the lysozyme.

With regard to factors (3) and (7), it is noted that while there are some working examples (1-6): for lysozyme a mediator of myocardial depression and andrenergic dysfunction in septic shock; and N,N',N'' triacetylglucosamine or N,N' diacetylchitobiose as an inhibitor of lysozyme and claims 1-16 are directed to a method of preventing or reducing the myocardial dysfunction and an inflammatory response and to inhibit lysozyme comprising administering an effective amount of an agent, it is not seen as sufficient to support the breath of the claims wherein an effective amount of any agent used to a cell or animal involving the inhibition of lysozyme.

With regard to factor (8), the relative skill in the art as it relates to a method of preventing or reducing the myocardial dysfunction and an inflammatory response and to inhibit lysozyme comprising administering an effective amount of an agent, is that of a Ph.D. or M.D. level.

Presently, the instant specification is not seen to provide an enabling disclosure for the scope of the invention as set forth in claims 1-16, which encompass a method of preventing or reducing the myocardial dysfunction and an inflammatory response and to inhibit lysozyme comprising administering an effective amount of an agent. It is noted that Law requires that the disclosure of an application shall inform those skilled in the art how to use applicant's alleged discovery, not how to find out how to use it for themselves, see In re Gardner et al. 166 USPQ 138 (CCPA 1970). In the instant case, the amount of experimentation needed to verify the efficacy of a method of preventing or reducing the myocardial dysfunction and an inflammatory response and to inhibit lysozyme comprising administering an effective amount of an agent, would indeed be voluminous and unduly burdensome in view of the teachings of the instant disclosure.

35 U.S.C. 103(a) rejection

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-16 are rejected under 35 U.S.C. 103(a) as being obvious over Valisena et al. (Valisena) (Microbiologica, 19, pages 25-30, 1996) in combination with Rand-Meir et al.

(Rand-Meir) (Biochemistry, vol.8, no.10, 4206-4214,1969) and Rubio et al. (Rubio) (Immunochemistry, vol.10, 361-364, 1973).

It is noted that the instant claims are examined in terms of the treatment of myocardial dysfunction and an inflammatory response comprising administering an effective amount of an agent that can inhibit lysozyme to a cell or animal in need thereof, as following:

Valisena teaches that a substance that can inhibit lysozyme should also interfere in the regulation of cell differentiation and the regulation of immune response, which are the major roles of said lysozyme (page 26, 1st col., 1st para.). Valisena discloses that hen egg-white lysozyme can be inhibited by the inhibitors such as chitotriose (tri-N-acetylglucosamine) and chitobiose (di-N-ectylglucosamine) and thus stimulating the immuno response (abstract and Figure 1 on page 27). It is noted that chitotriose and chitobiose are well known to have two or more N-acetylglucosamine units. Valisena also discloses that chitotriose is responsible for significantly enhancing antibody production in mice (page 26, 1st col. 2nd para. and Table 1 on page 27). Furthermore, Valisena discloses that lysozyme perform their regulatory function by interacting directly with immune competent cells by binding to specific receptors however an inhibitor such as N-acetyl-chito-oligosaccharide can inhibit the binding of endogenous lysozyme to its receptors on immune competent cells (page 29, 1st col., 2nd para.). Valisena is silent in disclosing specifically the treatment of the myocardial dysfunction and an inflammatory response by inhibiting the lysozyme with said agent however it is the inherent property

of an agent having at least two N-acetylglucosamine units to inhibit lysozyme thus effective in the treatment of the myocardial dysfunction and an inflammatory response.

Rand-Meir teaches that lysozyme binds chitin oligosaccharides to a series of subsites, three of which form a strong enzyme-inhibitor complex with chitotriose (page 4206, 1st col. 2nd para. to 2nd col. line 1 and Figure 1 on page 4207). Rand-Meir discloses the lysozyme-catalyzed cleavage of di N-acetylglucosamine derivative (page 4210, 1st col., under Discussion).

Rubio teaches the effect of lysozyme inhibitor N-acetyl-D-glucosamine (NAG) unable to avoid precipitation of the enzyme by its antibodies (abstract). Rubio discloses the inhibitory effects of NAG and antibodies on lysozyme wherein the antibody does not displace NAG from the complex of enzyme-inhibitor (page 362, Figure 1). Furthermore, Rubio discloses that an antibody can prevent NAG from reaching subsite C of lysozyme and conversely, NAG prevents antibody from neutralizing lysozyme (page 364, under Discussion, 2nd para.).

With regard to the treatment of myocardial dysfunction and an inflammatory response comprising administering an effective amount of an agent that can inhibit lysozyme to a cell or animal in need thereof of independent claims 1,7,13,14 and 16, it would be within the scope of the inherent properties of an agent having at least two N-acetylglucosamine (NAG) units to treat said conditions by inhibiting lysozyme.

It would have been obvious to person having ordinary skill in the art at the time the invention was made, that any agent comprising NAG can inhibit lysozyme as taught by

Valisena; Rand-Meir; and Rubio and thus can be used in the treatment of myocardial dysfunction and an inflammatory response in animal because Valisena; Rand-Meir; and Rubio references disclose the inherent property of an agent comprising NAG in the inhibition of lysozyme. The motivation is provided by Valisena, the prior art suggests that lysozyme perform their regulatory function by interacting directly with immune competent cells by binding to specific receptors however an inhibitor such as N-acetyl-chito-oligosaccharide can inhibit the binding of endogenous lysozyme to its receptors on immune competent cells (page 29, 1st col., 2nd para.).

Any inquiry concerning this communication or earlier communications from the

Examiner should be directed to Devesh Khare whose telephone number is (571)272-0653. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang, Supervisory Patent Examiner, Art Unit 1623 can be reached at (571)272-0627. The official fax phone numbers for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For

more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Devesh Khare, Ph.D.,J.D.
Art Unit 1623

November 27, 2006